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Dockets Management Branch
(HFA–305
Food and Drug Administration
5630 Fishers Lane
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Rockville, MD 20852

Docket 00D-1424

This comment addresses the Draft Guidance for Industry on Analytical Procedures and Methods Validation: Chemistry, Manufacturing, and Controls Documentation published August 30, 2000.

This document continues decades of confusion by FDA on when analytical methods need to be validated during product development.

The draft guidance states [Lines 213 – 214]: "The amount of information on analytical procedures and methods validation necessary will vary with the phase of the investigation (21 CFR 312.23(a)(7)), " then references other published guidance. The confusion arises from s a subtle distinction between the requirements for submission and the requirements to perform. 21 CFR section 211.194(a)(2) apparently requires some kind of method validation, and comment #49 to the September 29, 1978 final rule on CGMP indicated that the CGMP regulations apply in full to the manufacture of clinical supplies. Thus, the CGMP seemingly require method validation generally, but FDA seemingly doesn't want to see it until the application is filed; this interpretation of existing guidance is, however, inconsistent with the current draft [Lines 226-227].

In podium policy, FDA repeatedly states that methods used for investigational drugs must be qualified, not validated, but FDA has never clearly defined the distinction. In the rare inspections of clinical supply manufacturers, the policy is inconsistent. In general, FDA has stated from the podium that they expect a

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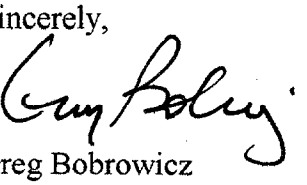
graded implementation of CGMP during product development, but no one in FDA has defined which CGMP requirements do not apply during manufacture of clinical supplies.

This guidance document under discussion should define which elements of method validation are and are not required during product development irrespective of the requirement to submit the supporting documentation, and, in tabular form, define when each requirement is effective. Important elements would include:

- Equipment qualification
- Software validation
- Inter-analyst and inter-laboratory precision
- Qualification of the reference standard
- An approved protocol with defined acceptance criteria
- An approved report demonstrating that the acceptance criteria were met.

Sincerely,



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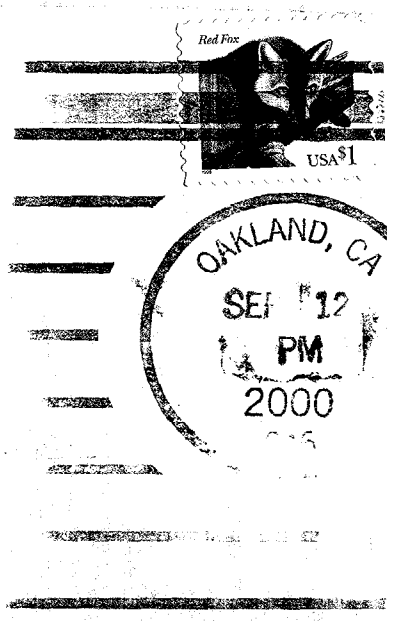

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